VARIABILITY IN COGNITIVE IMPAIRMENT OVER TIME IN PEOPLE WITH HIV AND MATCHED CONTROLS

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Background

Despite persistent reports of cognitive impairment (CI) in people with HIV (PWH) on antiretroviral therapy, limited data exist on the dynamics of change of CI over time.

Aim

To describe changes over 2 years in proportions of PWH and matched HIV-negative controls who are classified as having CI using a commonly-used definition of CI.

Methods

The COBRA cohort

- **123 PWH** aged ≥45, on antiretroviral treatment and with plasma HIV RNA <50 copies/mL for ≥1 year, recruited at HIV outpatient clinics in Amsterdam and London
- **77 HIV-negative controls** aged ≥45 with similar socio-demographic and lifestyle characteristics, recruited from sexual health centres in Amsterdam and London

The baseline study visit took place between January 2013 and October 2014 with follow-up visits approximately two years after (completed in June 2016).

Assessment of cognitive function

Cognitive function was assessed at both baseline and follow-up visits using a **standardised battery covering six domains** (Table 1).

Domain	Tests
Attention	WAIS-III letter-number sequencing; Paced auditory serial addition test
Executive function	Trail Making Test B; Wisconsin card sorting test
Language	Category (animals and occupations) and letter fluency
Memory	Rey Auditory Verbal Learning; WMS-IV Visual Reproduction
Motor function	Grooved pegboard; Finger tapping
Processing speed	Trail Making Test A; WAIS-III digit symbol; WAIS-III symbol search; Stroop colour-word test I and II

Table 1: Neuropsychological tests administered by cognitive domain

Definition of CI and reliable change over time

CI was defined using multivariate normative comparison (MNC)[1]: a simultaneous comparison of multiple cognitive test scores against those of a normative control sample, taking the correlations between tests into account.

A **statistically reliable change** (decline/improvement) over time (a change that is unlikely to have occurred by measurement error, practice effect or regression to the mean) was determined by applying the MNC to the differences between follow-up T-scores and those predicted by baseline T-scores, age and education.

Statistical analysis

Fisher's exact test was used to assess differences in the number of people moving over time from CI to no CI (and vice versa) between PWH and controls.

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Results

Median (IQR) or n (%)		PWH (n=123)	HIV-negative (n=77)	*p*
Age [years]		55 (50, 61)	57 (52, 64)	0.18
Male		114 (93%)	71 (92%)	0.90
Black-African		16 (13%)	1 (1%)	0.003
MSM		103 (84%)	60 (78%)	0.30
Years of education		14 (13, 16)	16 (14, 16)	0.22
Interval between testing [years]		2.0 (1.7, 2.2)	1.9 (1.7, 2.1)	0.20
Self-reported smoking	*Current smoker*	35 (28%)	19 (25%)	0.30
	Ex-smoker	53 (43%)	28 (36%)	
Self-reported alcohol use	*Current drinker*	96 (78%)	69 (91%)	0.06
	Previous drinker	15 (12%)	3 (4%)	
Recreational drug use (self-reported)		40 (32%)	17 (22%)	0.11
CD4⁺ count [cells/µL]		604 (472, 793)	N/A	
Duration of known HIV [years]		15 (9, 19)	N/A	
Nadir CD4 count [cells/µL]		170 (80, 230)	N/A	

Table 2: Characteristics of study participants at baseline

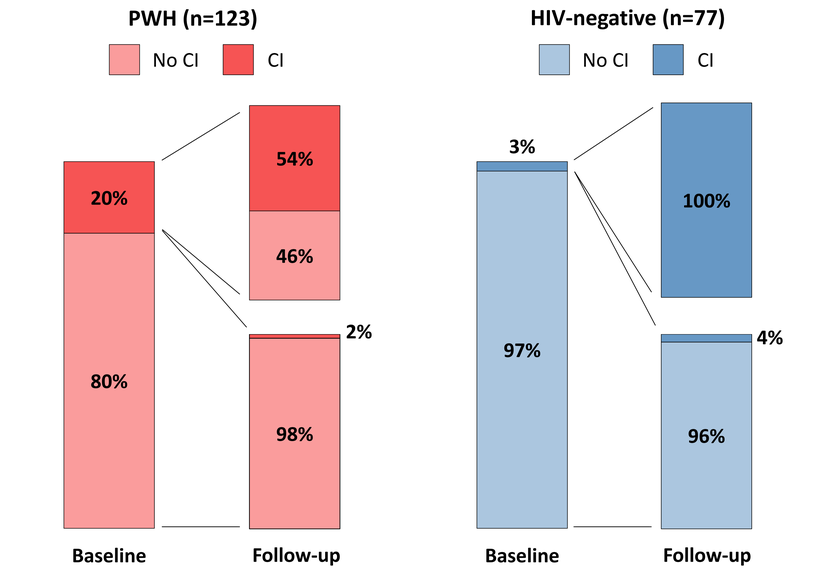

Figure 1: HIV-negative individuals and PWH with and without CI at baseline and follow-up

At baseline, 24 (20%) PWH and 2 (3%) controls had CI (p<0.001). Whilst none of the controls with CI at baseline improved to no CI at follow-up, 11/24 (46%) PWH moved from CI to no CI (p=0.49, Figure 1). Among those with no CI at baseline, 2/99 (2%) PWH and 3/75 (4%) controls moved to having CI (p=0.65).

Statistically reliable change in cognitive function

Among the 12 (10%) PWH and 5 (7%) controls who experienced a significant decline in cognitive function over two years (p=0.42), 6/12 (50%) PWH and 2/5 (40%) controls had no CI at both baseline and follow-up; 1/12 (8%) PWH and 2/5 (40%) controls moved from not having CI to have CI (Figure 2). Moreover, 14 (11%) PWH and 1 (1%) control had a reliable improvement over time (p=0.01), with 4/14 (29%) PWH improving from CI at baseline to no CI at follow-up.

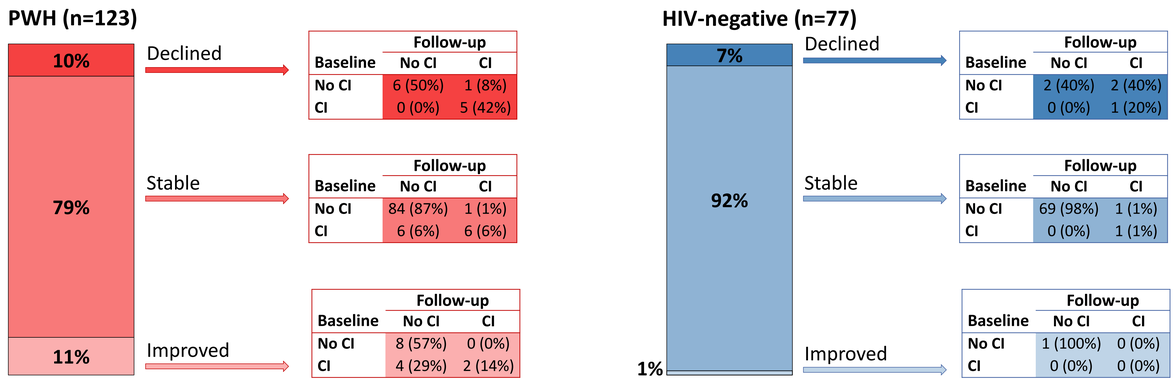

Figure 2: Proportion of PWH and controls showing a reliable improvement or decline, or remaining stable over time.

Conclusion

- A substantial proportion of PWH who were classified as having CI initially, did not meet the same criteria for CI after 2 years.
- Only less than half of both PWH and controls who significantly declined, met the definition of CI at both baseline and follow-up.
- Linkage of these dynamics of change in cognitive function with biomarker and neuroimaging findings may assist improving the understanding of the underlying pathogenic mechanisms and developing future targeted management approaches of PWH at risk of cognitive decline.

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[1] Schouten J et al. Determinants of reduced cognitive performance in HIV-1-infected middle-aged men on combination antiretroviral therapy. *AIDS* 30.7 (2016): 1027-1038.